

Serial No. 09/847,935
Reply of August 8, 2006

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Applicants are in receipt of the Office Action mailed May 8, 2006, and have the following comments.

Applicants gratefully thank the Examiner for withdrawing the 35 USC § 103(a) rejection of claims 60-63-65, 66, 72, 73, and 77 over Gil et al., US Patent No. 6,294,553).

Applicants have amended claim 60 to add a Markush group of fatty acid moieties. Support for this amendment can be found, e.g., at page 13 of the specification. The purpose of this amendment was solely to eliminate prostaglandins from being considered fatty acids, and no other narrowing of the claims, including the scope of equivalents, was intended or should be inferred thereby.

Claims 89 and 90 have been amended so as to make their language consistent and to provide antecedent basis. No surrender of subject matter is intended or should be inferred thereby.

Rejection pursuant to 35 USC §102(b)

The Office Action has rejected newly added claims 87 and 88 as allegedly anticipated by DeSantis, Jr. et al., U.S. Patent

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5,811,443. Applicants respectfully traverse this rejection for the following reasons.

Independent claim 87 is directed to a composition comprising in an aqueous medium, an ion-paired complex comprising a therapeutic component comprising an alpha adrenergic agonist, wherein the complex comprises a 3:1, 2:1, 1:1, 1:2 or 1:3 molar ratio of efficiency-enhancing component to therapeutic component, and an efficiency-enhancing component (EEC), wherein the EEC is selected from the group consisting of anionic polymers, fatty acids, and mixtures thereof, and is effective to enhance the movement of the therapeutic component across a lipid membrane, or a biological membrane under physiological conditions, each of said the enhanced effects being relative to the effect obtained with the therapeutic component without complexed efficacy enhancing component.

Claim 88 is the composition of claim 87 wherein the therapeutic component is an alpha adrenergic component.

The Office Action on page 4, states that DeSantis discloses, among other things, that the ratio of prostaglandin to clonidine is 1:1 to 1:10,000, and cites column 8, lines 14-17. The Office Action concludes the ratio of 1:1 meets the limitations of claims 87.

DeSantis does not, in fact, disclose the ratios set forth in claim 87. Claim 87 is drawn to a composition comprising a complex

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comprising a 3:1, 2:1, 1:1, 1:2 or 1:3 molar ratio of efficiency enhancing component to therapeutic component: that is, a ratio of how many molecules of the therapeutic component are associated with each molecule of efficiency enhancing component. By contrast, DeSantis is drawn to a weight ratio of clonidine to prostaglandin of between about 1:1 to about 10,000:1.

Additionally, the Office Action stated that the claim language of claim 87 "effective to enhance movement of the therapeutic component across a lipid membrane, or a biological membrane under physiological conditions, each of said the enhanced effects being relative to the effect obtained with the therapeutic component without complexed efficacy enhancing component" is a property of the composition. However, while Applicants agree that the quoted language is indeed a property of the present invention as claimed, the quoted language is a functional limitation (under which the composition can be tested, for example, against the same concentration of the therapeutic component without complexed efficiency enhancing component), rather than merely a listing of the properties of the claimed compositions. The Examiner has not cited any support, or taken official notice that all compositions comprising complexes between any therapeutic component and any fatty acid necessarily have this property.

More importantly, Applicants believe that the Office Action attempts to use the disclosure of Applicants' own patent application as a basis for finding anticipation in this case. Use

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of the Applicants' own disclosure against them in this manner is clearly an improper hindsight analysis.

An invention is anticipated if each and every element of the claimed invention is disclosed in a single prior art reference. See, e.g., *In re Paulsen*, 30 F.3d 1475, 31 USPQ2d 1671 (Fed. Cir. 1994) (emphasis added). This single anticipatory reference must place the person of ordinary skill in the art in possession of the claimed invention. *In re Spada*, 911 F.2d 705, ___, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990); *Akzo Nobel, N.V. v. U.S. International Trade Commission*, 808 F2d 1471, 1479), 1 USPQ2d 1241, 1245 (Fed. Cir. 1986).

In this case the cited prior art does not disclose a complex comprising a 3:1, 2:1, 1:1, 1:2 or 1:3 molar ratio of efficiency enhancing component to therapeutic component. For this reason alone, DeSantis does not anticipate claims 87 and 88.

Rejection pursuant to 35 USC §102(e)

The Office Action has rejected claims 87, 88, and 90 as being allegedly anticipated by Beck et al., U.S. Patent 6,358,935. Applicants respectfully traverse this rejection for the following reasons.

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The Office Action alleges that Beck discloses compositions comprising a complex of brimonidine (an alpha 2 agonist), sodium carboxymethylcellulose and cyclodextrin. Each of carboxymethylcellulose (CMC) and cyclodextrin are said to be EEC's by the Examiner. The Office Action alleges that the ratio of the therapeutic agent quinoxaline to the cellulose is 1:1 in example 1 (see Office Action at page 5.

Beck does not disclose a 1:1 molar ratio of therapeutic agent quinoxaline to EEC, whether CMC or cyclodextrin. In Example 1 the amount of brimonidine tartrate (quinoxaline) is 0.2% (w/v), and the amount of CMC is 0.5% (w/v). Since the molecular weights of the polymeric CMC and the polymeric cyclodextrin are not provided in Beck, the molar ratio of therapeutic component to EEC in Beck is not determinable.

As a result, Beck does not anticipate claims 87, 88 or 90, and Applicants respectfully request that the Examiner reconsider and withdrawn the outstanding rejection of these claims under 35 USC § 102.

Rejection pursuant to 35 USC §103(a)

The Office Action has rejected claims 60, 61, 64-66 and 68 as being allegedly obvious over DeSantis et al., U.S. Patent No. 5,811,443. Applicants hereby respectfully traverse this rejection for the following reasons.

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DeSantis is said to disclose at least one clonidine derivative and at least one prostaglandin. The Office Action alleges that prostaglandin is a fatty acid. Prostaglandins are derivatives of arachidonic acid, which is a 20-carbon fatty acid. See specification, page 13, last paragraph.

Claim 60 has been amended to specify that the EEC comprises a fatty acid selected from the group consisting of lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, lignoceric acid, palmitoleic acid, oleic acid, linoleic acid, linolenic acid, derivatives and mixtures thereof.

DeSantis, which does not describe or suggest a complex between a therapeutic agent and an EEC comprising a fatty acid selected from the group set forth above, thus does not describe or suggest the invention set forth in claim 60.

Since claims 61, 64-66 and 68 depend from claim 60, these claims are similarly not obvious in light of DeSantis.

Claims 60, 62, 63, 72, 73 and 77 were rejected as allegedly obvious over DeSantis and further in view of Gluchowski (US Patent No. 5,021,416). Applicants respectfully traverse this rejection for the following reasons.

The Office Action employs the same rationale for this rejection as for the rejection immediately above based on DeSantis

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alone, with the additional modification that Gluchowski is said to disclose quinoxaline, which is admittedly missing from DeSantis.

As stated above, claim 60 has been amended and cannot be read to include or even suggest the possibility of a prostaglandin EEC in complex with a therapeutic agent. For this reason claim 60 is not lacking in obviousness over DeSantis and Gluchowski. The remaining of the rejected claims are dependent from claim 60, and are therefore not lacking in obviousness either.

Claim 89 is rejected as being allegedly obvious over Beck et al. Applicants respectfully traverse this rejection for the following reasons.

As stated above with respect to the rejection under 35 USC § 102 over Beck, Beck does not disclose a 1:1 molar ratio of therapeutic agent quinoxaline to EEC, whether CMC or cyclodextrin.

In Example 1 the amount of brimonidine tartrate (quinoxaline) is 0.2% (w/v), and the amount of CMC is 0.5% (w/v). Since the molecular weights of the polymeric CMC and the polymeric cyclodextrin are not provided in Beck, the molar ratio of therapeutic component to EEC in Beck is not determinable.

For this reason Beck cannot be held to disclose or suggest the invention of claim 89, which is drawn to a composition comprising a complex, wherein the complex comprises a 3:1, 2:1, 1:1, 1:2 or 1:3 molar ratio of efficiency-enhancing component to therapeutic component.

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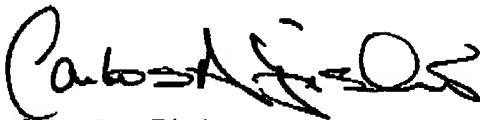
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CONCLUSION

For the foregoing reasons the claims are thought to be in condition for allowance, and the Applicants respectfully request that the Examiner issue a Notice to that effect. If the Examiner has any questions or comments, a telephone call to the undersigned is respectfully solicited.

No fee is thought to be due in connection with this communication, as it is being filed within the three month shortened statutory period. However, if Applicants are in error in this regard, kindly use Deposit Account 01-0885 for the payment of any charge now due.

Respectfully submitted,



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